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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,880	07/10/2003	Benjamin David Silverman	YOR920030162US1	2640
48062	7590	02/07/2008	EXAMINER	
RYAN, MASON & LEWIS, LLP 1300 POST ROAD SUITE 205 FAIRFIELD, CT 06824			NEGIN, RUSSELL SCOTT	
ART UNIT		PAPER NUMBER		
1631				
MAIL DATE		DELIVERY MODE		
02/07/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/616,880	SILVERMAN, BENJAMIN DAVID
	Examiner Russell S. Negin	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 31 October 2007.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,3-5,7-9,14,15,17 and 19-21 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,3-5,7-9,14,15,17 and 19-21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 31 October 2007 is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____	6) <input type="checkbox"/> Other: _____

## DETAILED ACTION

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 October 2007 has been entered.

Claims 1, 3-5, 7-9, 14-15, 17, are 19-21 are pending, and examined in this Office action.

### ***Drawings***

The amended drawings filed on 31 October 2007 are acceptable.

### ***Claim Rejections - 35 USC § 101***

The following 35 U.S.C. 101 Rejections are reiterated from the Office action of 29 March 2007:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3-5, 7-9, 14-15, 17, and 19-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility". Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.
- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant case, the claimed invention does not "transform" an article or physical object to a different state or thing because it is a method for calculating a global hydrophobic moment of a tertiary protein structure. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

*physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the*

*judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)*

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

Instant claims 1; 3-5, and 7-9 are drawn to a method for calculating a global hydrophobic moment of a tertiary protein structure. However, as claimed, the method does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer or a human mind without any communication to the outside world and without using or making available for use, the results of the computation. In an embodiment of the instant set of claims, the "outputting" step may cause the result to be presented to a user in the form of a carrier wave, which, *per se*, is not statutory. Thus, the instant methods of the claims do not produce any tangible result.

The instant claims are also drawn to an apparatus and article of manufacture for optimizing the structure of a protein. Claims 14-15, 17, and 19-20 are directed to a "device" comprising "units" which appear to be instructions for performing method/program steps. Furthermore, the article of manufacture in claim 21 comprises computer readable media. The computer readable media comprise instructions for performing a method. Although the specification gives tangible examples of computer

readable media (see page 12), the method performed by the computer and computer readable media does not produce a tangible result.

Consequently, with regard to all claims, the method to be performed does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer without any communication to the outside world and without using or making available for use, the results of the computation to a "user" (i.e. one performing the method). Thus, the instant methods of the claims do not result in a transformation of an article to a different state or thing, nor do they produce any tangible result, therefore the claims are directed to nonstatutory subject matter.

Response to Arguments:

Applicant's arguments filed 31 October 2007 have been fully considered but they are not persuasive.

Applicant argues that the amendments "outputting the global linear hydrophobic moment to at least one of a user, a display, a memory and one or more additional computers on a network," overcome the 35 U.S.C. 101 rejections. This is not found to be persuasive because this amendment still yields nonstatutory embodiments. For example, outputting results to a memory may yield a result that is only accessible to another computer and not a result that is tangibly accessible to a user.

***Claim Rejections - 35 USC § 112***

The rejections of claims 1-5, 7-9, 14-15, and 17-21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments filed on 31 October 2007.

**The following rejection is newly applied:**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5, 7-9, 14-15, 17, are 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 14, and 21 it is unclear how the correlation enhancing step relates to the remainder of each of the claims. For example, in claim 1, in the step of "enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric," both solvent accessibility and this enhanced correlation are not referred to in subsequent steps of the claim. Consequently, the interpretation of this claim would not be affected upon removal of this "enhancing" step (i.e. the claim can stand alone with the same meaning upon elimination of this step in each of the independent claims).

***Claim Rejections - 35 USC § 103***

The rejection of claims 1, 3-5, and 7-9 under 35 U.S.C. 103(a) as being unpatentable over Silverman in view of Clarke et al. is withdrawn in view of arguments filed by applicant on page 9-11 of the Remarks.

The rejection of claims 14-15, 17, and 19-21 under 35 U.S.C. 103(a) as being unpatentable over Silverman in view of Clarke et al. in further view of Michaud [USPAT 4,017,721] is withdrawn in view of arguments filed by applicant on page 11-12 of the Remarks.

**The following 35 U.S.C. 103 Rejection is newly applied:**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, 7-9, 14-15, 17, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eisenberg et al. [Nature, volume 299, 1982, pages 371-274] in view of Silverman [PNAS; April 24, 2001; volume 98, pages 4996-5001].

Claim 1 is drawn to a method for calculating a global hydrophobic moment of a tertiary protein structure comprising a plurality of residues, the method comprising the steps of:

--calculating a centroid of residue centroids;

--using the centroid of residue centroids as a spatial origin of a global linear hydrophobic moment;

--calculating a first-order hydrophobic moment;

--enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric;

--using the first order hydrophobic moment to define a global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global hydrophobic moment;

--using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure; and

--outputting the global linear hydrophobic moment to at least one or a user, a display, a memory and one or more additional computers on a network.

Claim 14 is drawn to the same subject matter as claim 1 wherein an apparatus is used for executing the method.

Claim 21 is drawn to the same subject matter as claim 1 wherein an article of manufacture is used for calculating a global hydrophobic moment of a tertiary protein structure.

Claims 3-4 and claims 19-20 are further limiting with the additional limitations that the correlation between the residue centroid magnitude and the residue solvent.

accessibility is enhanced by using an ellipsoidal metric and a solvent accessibility metric, respectively.

Claim 5 and claim 15 are further limiting with the additional limitation that the centroid of residue centroids represents a geometric center of the tertiary protein structure.

Claims 7-9 and claim 17 are further limiting with the additional limitations that the global linear hydrophobic moment characterizes the magnitude of amphiphilicity, direction of amphiphilicity, and identification of functional regions in the tertiary protein structure, respectively.

The article of Eisenberg et al. studies use of a first order helical hydrophobic moment to measure the amphiphilicity of a helix.

The abstract on page 371 of Eisenberg et al. quantifies the mean hydrophobic moment as a vector sum of all of the first order hydrophobic moments of the residues constituting the helix.

Figure 1 of page 372 of Eisenberg et al. illustrates a vector sum for a helix to determine a global (i.e. mean) hydrophobic moment for a protein helix. Each residue in the helix contributes a magnitude and direction of the global hydrophobic moment.

Figure 2 on page 374 of Eisenberg et al. plots the hydrophobic moments of helices of different proteins as a function of the degree of hydrophobicity/amphiphilicity of each of the helices in the study.

Figure 1 is also an output of the global linear hydrophobic moment for an alpha helix.

However, Eisenberg et al. does not use residue centroids as the origins in the hydrophobic moment calculations (instead, alpha carbons are used as reference points), Eisenberg et al. does not show correlation enhancement between residue centroid magnitude and solvent accessibility, and Eisenberg et al. does not show the computer hardware and software limitations of the instant claims.

The article of Silverman, "Hydrophobic moments of protein structures: Spatially profiling the distribution," describes how to calculate moments of tertiary protein structures.

In equation [12] on page 4997 of Silverman,  $r_i$  is the vector pointing to the centroid of residue  $i$  while  $r_c$  is the vector pointing to the centroid of the entire protein molecule (i.e. the geometric center of the protein).

In equation [13] on page 4998 of Silverman, a first order hydrophobic moment imbalance about the entire protein is derived, accounting for hydrophobicity and solvent accessible surface area. Each centroid of every protein residue contributes to this global moment.

In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

Figure 6 on page 5000 of Silverman shows how an arm of the protein can be identified as it falls outside the ellipse characterizing the hydrophobic moment of the protein.

Pages 4998-5000 of Silverman illustrate the computation of a hydrophobic moment for entire proteins.

Additionally, page 4998, column 2 teaches the obtaining of protein structures from the Internet, and page 5000, column 2, paragraph 2 teaches obtaining protein structures from the PNAS website.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the helical hydrophobic moment study of Eisenberg et al. by use of the hydrophobic moment study of Silverman wherein the motivation would have been that using residue centroids instead of atomic points yields a more ideal overall shape and moment of the protein (see first full paragraph of column 1 on page 4998 of Silverman). Additionally, automation of the process of Eisenberg et al. on the internet provides a faster and more efficient means of executing the claimed invention.

Response to Arguments:

Applicant's arguments with respect to claims 1, 3-5, 7-9, 14-15, 17, and 19-21 have been considered but are moot in view of the new ground(s) of rejection.

**Conclusion**

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices

published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).  
The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN  2/1/08  
1 February 2008

/Marjorie A. Moran/  
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2/4/08